IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

GENENTECH, INC. and ROCHE PALO ALTO LLC,

Plaintiffs,

v.

SANDOZ INC.,

Defendant.

No. C 11-01925 JSW
No. C 11-02410 JSW

CLAIM CONSTRUCTION ORDER

GENENTECH INC. and ROCHE PALO ALTO LLC,

Plaintiffs,

v.

APOTEX INC.,

Defendant.

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The Court has been presented with a technology tutorial and briefing leading up to a hearing pursuant to *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996). This Order construes the single claim term selected by the parties, which appears in claim one of the patent at issue in this case, United States Patent No. 6,083,953 ("the '953 Patent") which protects the proscription drug VALCYTE®, containing the active ingredient valganciclovir hydrochloride.

The prescription medication is employed by patients with immune deficiency, including recipients of certain organ transplants and patients suffering from advanced HIV infection. These patients are susceptible to infection by viruses such as cytomegalovirus, with potentially devastating consequences, such as blindness and even death. Prior to the invention, the treatment was ganciclovir which has limited bioavailability when given orally, so it was administered intravenously or by injection directly into the eye. The inventors of the '953 Patent made a compound which combined one molecule of ganciclovir joined by an ester linkage to one molecule of the amino acid L-valine. This form of ganciclovir is well absorbed orally and is metabolized into the bloodstream for effective treatment of cytomegalovirus in immune-compromised patients.

The parties dispute the meaning of one phrase – "in crystalline form" – that appears in claim 1 of the '953 Patent. The Court shall address additional facts as necessary in the remainder of this Order.

ANALYSIS

A. Legal Standard.

"It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004). The interpretation of the scope and meaning of disputed terms in patent claims is a question of law and exclusively within the province of a court to decide. *Markman*, 517 U.S. at 372. The inquiry into the meaning of the claim terms is "an objective one." *Innova/Pure Water*, 381 F.3d at 1116. As a result, when a court construes disputed terms, it "looks to those sources available to the public that show what a person of skill in the art would have understood the disputed claim language to mean." *Id*. In most cases, a court's analysis will focus on three sources: the claims, the specification, and the prosecution history. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). However, on occasion, it is appropriate to rely on extrinsic evidence regarding the relevant scientific principles, the meaning of technical terms, and the state of the art at the time at the time the patent issued. *Id.* at 979-981.

The starting point of the claim construction analysis is an examination of the specific claim language. A court's "claim construction analysis must begin and remain centered on the claim language itself, for that is the language that the patentee has chosen to particularly point out and distinctly claim the subject matter which the patentee regards as his invention." *Innova/Pure Water*, 381 F.3d at 1116 (internal quotations and citations omitted). Indeed, in the absence of an express intent to impart a novel meaning to a term, an inventor's chosen language is given its ordinary meaning. *York Prods., Inc. v. Cent. Tractor Farm & Family Center*, 99 F.3d 1568, 1572 (Fed. Cir. 1996). Thus, "[c]laim language generally carries the ordinary meaning of the words in their normal usage in the field of the invention." *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1367 (Fed. Cir. 2003); *see also Renishaw v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1248 (Fed. Cir. 1998) (recognizing that "the claims define the scope of the right to exclude; the claim construction inquiry, therefore, begins and ends in all cases with the actual words of the claim"). A court's final construction, therefore, must accord with the words chosen by the patentee to mete out the boundaries of the claimed invention.

The court should also look to intrinsic evidence, including the written description, the drawings, and the prosecution history, if included in the record, to provide context and clarification regarding the intended meaning of the claim terms. *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1324-25 (Fed. Cir. 2002). The claims do not stand alone. Rather, "they are part of 'a fully integrated written instrument.'" *Phillips v. AWH Corp.*, 415 F.3d 1303, 1315 (Fed. Cir. 2005) (en banc) (quoting *Markman*, 52 F.3d at 978). The specification "may act as a sort of dictionary, which explains the invention and may define terms used in the claims." *Markman*, 52 F.3d at 979. The specification also can indicate whether the patentee intended to limit the scope of a claim, despite the use of seemingly broad claim language. *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.*, 242 F.3d 1337, 1341 (Fed. Cir. 2001) (recognizing that when the specification "makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims of the patent, even though the

language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question").

Intent to limit the claims can be demonstrated in a number of ways. For example, if the patentee "acted as his own lexicographer," and clearly and precisely "set forth a definition of the disputed claim term in either the specification or prosecution history," a court will defer to that definition. *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002). In order to so limit the claims, "the patent applicant [must] set out the different meaning in the specification in a manner sufficient to give one of ordinary skill in the art notice of the change from ordinary meaning." *Innova/Pure Water*, 381 F.3d at 1117. In addition, a court will adopt an alternative meaning of a term "if the intrinsic evidence shows that the patentee distinguished that term from prior art on the basis of a particular embodiment, expressly disclaimed subject matter, or described a particular embodiment as important to the invention." *CCS Fitness*, 288 F.3d at 1367. For example, the presumption of ordinary meaning will give way where the "inventor has disavowed or disclaimed scope of coverage, by using words or expressions of manifest exclusion or restriction, representing clear disavowal of claim scope." *Gemstar-TV Guide Int'l Inc. v. ITC*, 383 F.3d 1352, 1364 (Fed. Cir. 2004). The disclaimer in the prosecution history must be "clear and unmistakable." *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1325-26 (Fed. Cir. 2003). Likewise, the specification may be used to resolve ambiguity "where the ordinary and accustomed meaning of the words used in the claims lack sufficient clarity to permit the scope of the claim to be ascertained from the words alone." *Teleflex*, 299 F.3d at 1325.

However, limitations from the specification (such as from the preferred embodiment) may not be read into the claims, absent the inventor's express intention to the contrary. *Id.* at 1326; *see also CCS Fitness*, 288 F.3d at 1366 ("[A] patentee need not 'describe in the specification every conceivable and possible future embodiment of his invention.'") (quoting *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1344 (Fed. Cir. 2001)). To protect against this result, a court's focus should remain on understanding how a person of ordinary skill in the art would understand the claim terms. *Phillips*, 415 F.3d at 1323.

If the analysis of the intrinsic evidence fails to resolve any ambiguity in the claim language, a court then may turn to extrinsic evidence, such as expert declarations and testimony from the inventors. *Intel Corp. v. VIA Techs., Inc.*, 319 F.3d 1357, 1367 (Fed. Cir. 2003) ("When an analysis of *intrinsic* evidence resolves any ambiguity in a disputed claim term, it is improper to rely on extrinsic evidence to contradict the meaning so ascertained.") (emphasis in original). When considering extrinsic evidence, a court should take care not to use it to vary or contradict the claim terms. Rather, extrinsic evidence is relied upon more appropriately to assist in determining the meaning or scope of technical terms in the claims. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583-84 (Fed. Cir. 1996).

Dictionaries also may play a role in the determination of the ordinary and customary meaning of a claim term. In *Phillips*, the Federal Circuit reiterated that "[d]ictionaries or comparable sources are often useful to assist in understanding the commonly understood meanings of words...." *Phillips*, 415 F.3d at 1322. The *Phillips* court, however, also admonished that district courts should be careful not to allow dictionary definitions to supplant the inventor's understanding of the claimed subject matter. "The main problem with elevating the dictionary to ... prominence is that it focuses the inquiry on the abstract meaning of the words rather than on the meaning of claim terms within in the context of the patent." *Id.* at 1321. Accordingly, dictionaries necessarily must play a role subordinate to the intrinsic evidence.

In addition, a court has the discretion to rely upon prior art, whether or not cited in the specification or the file history, but only when the meaning of the disputed terms cannot be ascertained from a careful reading of the public record. *Vitronics*, 90 F.3d at 1584. Referring to prior art may make it unnecessary to rely upon expert testimony, because prior art may be indicative of what those skilled in the art generally understood certain terms to mean. *Id.*

B. Claim Construction.

The parties dispute the meaning of one phrase – "in crystalline form" – that appears in claim 1 of the '953 Patent. Claim one recites:

What is claimed is:

1. The compound 2-(2-amino-1,6-dihydro-6-oxo-purin-9-yl)methoxy-3-hydroxy-1-propanyl-L-valinate hydrochloride [valganciclovir hydrochloride] *in crystalline form*.

('953 Patent at 30:41:45.)

Plaintiffs Genentech and Roche Palo Alto argue that the phrase "in crystalline form" must be construed by this Court to mean "in a physical form having molecules arranged in a regularly repeating three dimensional pattern." (Joint Claim Construction and Pre-hearing Statements at 2.) Defendants Apotex Inc. and Sandoz, Inc., on the other hand, argue that the phrase should be construed to mean "*manufactured or* prepared in a stable, solid physical form having molecules arranged in a regularly repeating three dimensional pattern (*excluding any amorphous, semi-amorphous, partially ordered, or unstable forms*)." (*Id.*)[1]

There is no dispute that the crystalline state is characterized by a highly ordered arrangement of molecules in a three dimensional pattern. The key dispute between the parties is the timing of the compound's cystallinity. Defendants contend that the claim term "in crystalline form" requires that the patented valganciclovir hydrochloride be produced or manufactured in a stable crystalline form. Plaintiff argues that the term should be given its clear, unambiguous scientific meaning, without importation of a timing limitation or recitation of a process step with regard to the compound's method of manufacture or preparation. The Court finds that the invention specifically claims the crystalline form of the material and the inventors, in the course of the prosecution history, clearly distinguish prior art in which valganciclovir hydrochloride was disclosed in amorphous, not crystalline, form.

1. The Specification Requires the Material in Stable, Crystalline Form.

The Court is persuaded that the specification of the '953 Patent makes clear that the claim term "in crystalline form" requires that the drug be formulated as such. The specification clearly distinguishes crystalline from noncrystalline material based on the ease with which one can manufacture a stable oral dosage. The specification distinguishes the prior art which

[1] The italicized portions are requested in addition by Apotex, Inc. Both defendants, however, agreed to abandon the term "solid" as redundant. The Court finds both the italicized phrase and the term "solid" to be unnecessary.

consisted in noncrystalline materials as "difficult to process for the manufacture of oral pharmaceutical dosage forms." ('953 Patent at 3:32-34.)

The specification further discloses that the task of preparing the compound in crystalline form carries a "decisive advantage" over the prior art "non-crystalline materials" because "pharmaceutical formulations can be more easily produced with a crystalline material. A crystalline material can be processed efficiently and is susceptible of being more reproducibly characterized than a non-crystalline material, and the quality of the crystalline materials of the invention can be much more readily ascertained than that of non-crystalline materials." (*Id.* at 21:21-31.) Thus, once again, the specification makes a clear distinction between the purported invention which requires the material to be in crystalline form in order to create a stable oral dosage. It is clear from the language of the specification that the invention sought to solve the pre-existing problem of the drug in a non-stable oral formulation. *See CVI/Beta Ventures, Inc. v. Tura LP*, 112 F.3d 1146, 1160 (Fed. Cir. 1997) ("In construing claims, the problem the inventor was attempting to solve, as discerned from the specification and the prosecution history, is a relevant consideration.") (citations omitted). Although the claim term is quite broad, the specifications make clear that the broad inclusion of both metastable amorphous materials would be an error. *See SciMed Life*, 242 F.3d at 1341 (noting that when the specification "makes clear that the invention does not include a particular feature, that feature is deemed to be outside the reach of the claims in the patent, even though the language of the claims, read without reference to the specification, might be considered broad enough to encompass the feature in question").

In this case, the Court is persuaded that the specification is clear that the invention was intended to claim a stable form of valganciclovir hydrochloride at its inception in order to provide a stable oral dosage of the drug. In this regard, the Court also finds that the prosecution history is elucidating in that it clearly disavows the prior incarnation of the drug in its amorphous, or non-crystalline, form.

2. The Prosecution History Clearly Disclaims Amorphous Prior Art.

During the prosecution of the '953 Patent, the inventors initially sought to obtain claims that were broader, to include valganciclovir hydrochloride without regard to whether it was initially in its amorphous or crystalline form. However, the patent examiner rejected such broad claims under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,043,339 ("Beauchamp Patent"), which claimed the material in its amorphous form. The patent examiner only granted the application of the '953 Patent upon the addition of the technical requirement that the valganciclovir hydrochloride be "in crystalline form."

In response to the rejection for anticipation, the applicants of the '953 Patent disclaimed the previous amorphous incarnation of valganciclovir described in the Beauchamp Patent. The applicants of the '953 Patent, in an explicit effort to distinguish their claimed invention from the amorphous prior art, amended their application to state:

> However, there is a more fundamental aspect to be considered. The bis esters described by Beauchamp are non-crystalline materials which are difficult to process for the manufacture of oral pharmaceutical dosage forms .... Crystallinity of a drug is not only important for achieving better purification of the mono-L-valyl ester itself ... but also is decisive for the stability of oral formulations.
> ...
> For the drug formulator it is thus preferable to work with the form which has the lowest energy state, and therefore, is the most stable state, which is a crystalline rather than an amorphous form. Crystallization of a metastable form is well recognized as being catastrophic to the quality of an oral dosage form, such as a tablet. Use of a stable crystalline form avoids this risk.

(Declaration of Andy J. Miller ("Miller Decl."), Ex. 5 at 14-16.) The applicants specifically explained that the original amorphous form of valganciclovir was distinguishable in that its unstable form, even when subsequently crystallized, was "catastrophic" to the quality of the claimed invention's oral dosage form.

In addition, the applicants specifically argued to the patent examiner that even if prior art amorphous compounds later converted to crystalline form, which often happened, the resulting crystalline forms would not anticipate the "stable" crystalline form. The applicants contended that later-converted, as opposed to properly manufactured, crystalline forms are inherently unstable. The applicants clearly acknowledged the common physiological

conversion of amorphous to crystalline states, and claimed the benefits of the crystalline state in origin. The applicants, in response to the initial rejection of their broader claims, stated:

> It is well-known that drugs are most easily purified through a process of controlled re-crystallization, which allows growth of pure crystals from a saturated solution. Precipitation of an amorphous form does not offer this advantage of purification of the drug as it is isolated. A crystalline form of an active ingredient is therefore preferred as offering a more precisely purified material than an amorphous form.
> ...
> If the active drug only occurs in amorphous and thus metastable form, there is a high risk over the expected length of the shelf life of a product that it will convert to a crystalline form, which is likely to have physico-chemical, pharmaceutical and biological properties that are changed in comparison with the active substance in amorphous form.

(*Id.* at 15-16.)

In their efforts to distinguish the prior art, the applicants of the '953 Patent clearly disavowed the prior art as either an amorphous form of valganciclovir or an amorphous form that can later convert to crystalline form. The applicants stated that use of a stable crystalline, as opposed to a crystalline form that was initially amorphous, avoids the risk of catastrophic quality of the oral dosage form. Again, the applicants' amendment reads:

> For example, tablet disintegration or dissolution are pharmacopoeial properties which are expected to remain constant over the entire shelf life of a tablet. If the phase change occurs, it is most likely that the tablet with the crystalline active substance will show a tablet disintegration or dissolution behavior different from that of a tablet with an amorphous active substance.

(*Id.* at 16.)

Accordingly, the Court is compelled to adopt the narrow construction of a claim term where, as here, the inventors, in order to overcome a prior art rejection, necessarily disclaimed an examiner's interpretation of a limitation. *See Southwall Technologies, Inc. v. Cardinal IG Vo.*, 54 F.3d 1570, 1576-77 (Fed. Cir. 1995) (holding that patentees limited their claim scope where they necessarily disclaimed an examiner's interpretation of a limitation in order to overcome a prior art rejection); *see also Omega Eng'g*, 334 F.3d at 1324 ("[W]here the patentee has unequivocally disavowed a certain meaning to obtain his patent, the doctrine of prosecution disclaimer attaches and narrows the ordinary meaning of the claim congruent with the scope of the surrender.")

Throughout the prosecution history, the applicants clearly emphasized the criticality of a crystalline form and urged that the ability to process the valganciclovir hydrochloride in its stable crystalline form was both preferable and critical to its "pharmaceutical processing into dosage forms." (*Id.* at 16-17.) The applicants repeatedly disclaimed the prior art which "does not include *crystalline* GMVH [valganciclovir], since Beauchamp shows no compounds in crystalline form. ... none of the compounds prepared by Beauchamp were stated to have been prepared in crystalline form, so there is no suggestion in Beauchamp of the inherent crystallinity of such compounds." (Miller Decl., Ex. 13 at 4 (emphasis in original).) It was only through the addition of the specific term at issue – "in crystalline form" – that the patent examiner ultimately decided to issue the '953 Patent. It was only upon the applicants' clear disavowal of the pre-existing amorphous form – and an amorphous form that could convert to crystalline form – that the patent was granted.

During oral argument on the claims construction, Plaintiffs contended that the applicants did not need to differentiate their crystalline form of valganciclovir as crystalline at inception because the Beauchamp Patent simply did not anticipate a crystalline form at all and only explicitly claimed the amorphous form of valganciclovir. However, beside the prosecution history which clearly disclaims metastable forms of valganciclovir, including amorphous forms that convert to crystalline, the Court finds that the claims in the patent serve the function of public notice. The claims are supposed to provide to the public what it is that the patentees invented in exchange for the patentee's rights to exclude other people from practicing their invention. In addition, the prosecution history, replete with the forfeiture of the broad claims definition proposed by Plaintiffs, is "inimical to the public notice function provided by the prosecution history." *Hockerson-Halberstadt, Inc. v. Avia Group International, Inc.*, 222 F.3d 951, 957 (Fed. Cir. 2000). Prosecution disclaimer "promotes the public notice function of the intrinsic evidence and protects the public's reliance on definitive statements made during prosecution." *Omega Eng'g*, 334 F.3d at 1323 (citing *Digital Biometrics, Inc. v. Identix, Inc.*, 149 F.3d 1335, 1347 (Fed. Cir. 1998)). Once a patent is issued, the claims define the

boundaries of its protection and give notice to the public of those boundaries. *See, e.g., Model Jury Instructions: Patent Litigation,* 2005 A.B.A. Sec. Litigation 7–9.

The Court is persuaded that it is not reasonable to assume that the patent granted rights to an amorphous form of valganciclovir which at some unknown point and by unknown process metastasizes to crystalline form. This would undercut the essential and stated purpose of the invention of valganciclovir hydrochloride in crystalline form specifically protected by the '953 Patent. Accordingly, the Court construes the term "in crystalline form" to mean: "Prepared in a stable physical form having molecules arranged in a regularly repeating three dimensional pattern."

CONCLUSION

Based on the analysis set forth above, the Court adopts the foregoing construction of the disputed phrase. The parties are ordered to submit a further joint case management report pursuant to Patent Standing Order ¶ 13 by no later than August 3, 2012.

IT IS SO ORDERED.

Dated: July 9, 2012

JEFFREY S. WHITE
UNITED STATES DISTRICT JUDGE